

Dr. D. R. Schamburov, of the Neuropsychiatric Institute, Moscow, Russia,¹ injected rabbits with heat-killed *B. typhosus* by the subcutaneous, intraperitoneal and subdural routes. By injecting the vaccine directly into the cerebrospinal fluid the agglutinin content of this fluid was increased a hundred-fold over that obtained by any other method of immunization. The locally formed or locally mobilized antibodies remaining at this relatively high titer for at least two months.

Emboldened by this result, he applied subarachnoidal vaccination to the treatment of "infectious chorea." Injection of 0.1 cubic centimeters of his locally standardized streptococcus vaccine by lumbar puncture was followed by sharp pains in the legs and marked rise in body temperature. Following these transient symptoms "the disease ran an unusually favorable course." Schamburov, believes his favorable result justifies further study of subarachnoid vaccine therapy.

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Anthelmintic Properties of Certain Alkyl Resorcinols.—Two alkyl resorcinol derivatives, hexyl- and heptylresorcinol, have been tried successfully by Lamson and his associates¹ in the treatment of ascariasis and uncinariasis during the past year. While it is true that the presence of ascarids may not greatly disturb their human host, mechanical intestinal obstruction may occur or the parasites may open the way for other secondary invaders. Ascariasis is indigenous in the temperate zone, and in some southern states almost half the rural population is infested. Hookworm, likewise, is very prevalent in the southern and southeastern parts of this country, and is far more serious a problem. A progressive anemia, marked emaciation, and general debility are noted in patients suffering from mass hookworm infection.

Many anthelmintics have been tried in the past with varying degrees of success. Carbon tetrachlorid is effective in removing 95 to 100 per cent of hookworms from infested hosts, according to Lamson, Minot, and Robbins.² Cases of intoxication occur, however, which are neither preventable nor susceptible to treatment. These workers demonstrated that toxicity may occur when mechanical obstruction by ascarids is present, when the patient is an alcoholic, when there is undigested food in the stomach, or when calcium deficiency exists. Similar difficulties have followed the use of chenopodium oil (or its active principle "ascaridol") in ascariasis. Fatalities have resulted from the administration of therapeutic doses of these agents, and although such accidents are rare they seriously handicap extensive use of this form of treatment. In the face of these difficulties therapy in the field cannot be employed without endangering life, which necessitates the administration of these agents under carefully controlled hospital conditions.

In an effort to find a nontoxic yet effective anthelmintic, Lamson and his group in Nashville, Tennessee, tried hexyl- and heptylresorcinols with interesting results in the laboratory and clinically. Two conditions must be fulfilled, however, in controlling mass infestation, namely, single oral doses must give a maximum percentage of cures, and secondly, the therapeutic doses must not lie within the lethal range of the drug.

Both alkyl derivatives are irritating to the gastro-enteric tract, causing a burning sensation in the stomach, and in dogs crystalline hexylresorcinol produces small submucosal hemorrhages. Combined with the protein of food the agent is more toxic, and in alcoholic solution it penetrates more deeply into the tissues than when crystals are used. Leake et al.³ have observed that the toxicity of the alkyl resorcinols increases with increase in the number of carbon atoms in the straight carbon chain, in experimental animals. Tissue changes may occur, following lethal doses in rabbits, notably focal necrosis in the kidneys and hyaline degeneration of the cells lining the tubules.

Hexylresorcinol should be given in gelatin capsules, washed down with water under fasting conditions, according to Lamson. Elliott and Barbour⁴ have shown that hexylresorcinol is absorbed in the small intestine and is rapidly excreted in the urine. Doses of one gram three times a day over a ten-week period in normal adults cause no untoward symptoms, according to Leonard's experience.⁵ Lamson recommends single oral doses of one gram in ascariasis, and was able to remove 90 to 100 per cent of the parasites in twenty patients with this dose. He feels "justified, therefore, in suggesting crystalline hexylresorcinol as an ascaricide in spite of its irritant properties."

The agent has been proposed by the same authors also in the treatment of hookworm disease. Similar doses removed 90 per cent of the worms in a carefully observed group of patients. Food taken before or immediately after treatment caused nausea and vomiting in a few cases. Oil solutions were effective but disagreeable to take. In another test group heptylresorcinol ("dihydranol") was employed by Brown,⁶ who was again successful in treating worm infestation in a relatively large number of cases. This author gave single doses of one gram over an extended period to a total dosage of seventy grams of the drug to five adults without exhibition of toxicity. These drugs should be studied clinically in tapeworm infestation.

Preliminary clinical reports indicate that hexyl- and heptylresorcinol are superior to other anthelmintics now in use, and while they are not entirely free from toxicity in therapeutic doses, the resultant untoward effects are transient and not severe. Irritative properties must be appreciated, however, and efforts should be made to reduce these side actions to a minimum so that the agents may be used in mass treatment.*

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¹ Schamburov, D. A. Zur Frage der Antikörperbildung im Subarachnoidalraum. Ztschr. f. Hyg. u. Infektionskr., cxi, 278, April 1930.

* For references see page 144.